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# BIOLOGICAL RESEARCH IN SPACE (SOME CONCLUSIONS AND PROSPECTS)

Gazenko, O. G., Il'in, Ye. a. and Parfenov, G. P.

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16. Abstract

The main Soviet biomedical experiments conducted since the beginning of space flight are reviewed; on the basis of their results, it is concluded that prolonged manned space flight is possible, although certain apparently reversible changes in vital processes have been noted. The experiments are divided into four groups: research on mammals and turtles, on insetcs and amphibians, on plants, and on microorganisms and tissue cultures. In these experiments, the genetic effect of cosmic ionizing radiation and other factors of space environment, and the effect of weightlessness are stressed; the latter is at present the most pertinent factor. Six aspects of the action of weightlessness have been proven: 1) weightlessness chiefly affects body systems having a gravity-related function, 2) it does not evoke genetic mutations, 3) it does not

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determine the development of centrolecithal eggs having a holoblastic embryogenesis, 4) it does not affect bacteria cells and intracellular processes, 5) it does not affect cells in which metabolic processes are either very slow or suspended, and 6) 6) there is no direct correlation between the duration of exposure to weightlessness and the intensity of any changes observed in the organism. Weightlessness also does not appear to affect intracellular structure and processes; however, this has not been conclusively proven experimentally. The role of space biology in the determination of the univeral laws of vital processes is discussed; in reference to this, the authors mention the theory that gravity is essential for the evolution of higher forms of life, but no definite opinion on the theory is given.

BIOLOGICAL RESEARCH IN SPACE
(SOME CONCLUSIONS AND PROSPECTS)

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and Parfenov, G. P.

Man's exploration of space is doubtless one of the most remarkable and exciting achevements in his history. /461

As man has conquered his native planet, the unconcious desire for expanded settlement has gradually congealed in the thought of travel outside the Earth, of penetration into space. The accumulation of astronomical knowledge and the development of understanding of the actual physical picture of the universe have made voyages in space ever less fantastic and more possible.

As long ago as 1908, C. E. Tsiolkovskiy set forth the idea that after the creation of an artifical Earth satellite capable of returning unharmed to the Earth, the next step would be solution of the biological problems related to life support of spacecraft crews. Then, the scientist believed, many "rocket generations" would be put in orbit near the Earth, space stations maintaining continuous communications with out planet. However, he believed all this to be merely the forerunner of the "extra-atmospheric activity" of man which, he believed, would consist of several periods. The first period could be called the time of reconnaissance and study. During this period, man will learn to move about within the solar system. Then will come the time of colonization near our star. The colonization of the solar system will cause a grandiose scientific, technical and industrial boom, a prerequisite for the third period.

These were the great prospects drawn by the founder of astronautics, many of whose scientific visions have already come to pass. Doubtless, the tremendous capabilities and resources of space will belong to man.

The outstanding scientific and technical achievements of the past decades, primarily astronautics and space science, have thus led to the appearance of a new area of science -- space biology. /462
In new, rapidly developing areas of knowledge, it is difficult to define the limits of their competence and interests. From our point of view, space biology can at present be defined as an independent section of biology, studying the following main problems: 1) the vital activity and behavior of terrestrial organisms under conditions of space and space flight (exophysiology); 2) the propagation, development and evolution of life in the universe (exobiology); and 3) the biological principles and methods of creating a medium for habitation in spacecraft and planetary space stations (closed system ecology).

Until recently, the methods of biology allowed the phenomena of life to be studied within the strictly limited spatial limits of the biosphere of the Earth and within a somewhat less limited time frame. This is possibly one of the reasons that no universal laws such as the laws of physics have yet been discovered in biology.

The final goal of space biology, obviously, must be the establishment of laws controlling the development and evolution of life. In this aspect, we are interested by the seemingly paradoxical hypothesis that the evolution of higher forms of life requires a force of gravity similar to that of the Earth. There are possible direct experimental approaches to test this hypothesis. In case of a positive experimental confirmation of this hypothesis, the range of astronomical objects where intelligent life is possible will be greatly reduced. Naturally, space biology could develop only after the primary tool required for the accumulation of scientific facts in its area of competence was developed, i. e. only after controlled flight vehicles capable of achieving escape velocity and leaving the Earth were invented.

Flights into space allow us to study nature and the properties of living organisms by new, earlier impossible methods and open areas of investigation in which biological theories do not provide predictions to be proven.

The new environmental factors arising during space flights, such as extended weightlessness, the combined action of weightlessness and ionizing radiation, the absence of circadian rhythm and the elevated radiation background created by high-energy particles, of essential importance for biologists, cannot as yet be artificially produced on Earth.

These factors have the following peculiarities, making their study of exceptional biological interest. First of all, the action of these factors during space flights is continuous and practically unchanged. Secondly, terrestrial organisms have not encountered them throughout their entire history of existence and evolution. Finally, exposure to their action does not cause immediate death or acute pathology, so that precise and varied biological experiments are possible. Consequently, the specifices of the primary environmental factors involved in space flights allow a unique approach to the study of such cardinal questions of biological science as the roll of the force of gravity in the development of life and the realization of vital processes, the determinism of ontogenesis, the authenticity of biolotical evolution on Earth, etc.

Experimental biological studies in the upper layers of the atmosphere and in space have been conducted in our country for almost 40 years. The goals of these studies have changed repeatedly as new problems have arisen before science and mankind as man's knowledge of the space environment has increased and in con- /463
nection with the practical demands of space travel.

The studies of the 30's and 40's were evoked and stimulated by two scientific discoveries -- the discovery of cosmic radiation on the surface of the Earth and the undeniable proof of the mutagenic activity of ionizing radiation. When these discoveries were made, it was assumed that so-called spontaneous mutations of living organisms arise as a result of the influence of natural ionizing radiation on the organisms which, consequently, must be an important factor in biological evolution. Therefore, studies of this period were intended to clarify the influence of cosmic ionizing radiation on the evolutionary process.

This problem attracted the attention of many great biologists, including N. K. Kol'tsov, N. V. Timofeyev-Resovskiy, G. A. Nadson, G. G. Frizen, G. D. Meller and others. Since studies performed on the surface of the Earth yielded only modest results, it was assumed that the question of the genetic effectiveness and evolutionary significance of cosmic radiation could be solved by placing the experimental biological objects on the peaks of high mountains or by lifting them into the stratosphere by means of balloons.

The culminating point of investigations of this period were the genetic experiments onboard the "SSSR-1-BIS" stratostat.

Along with the studies of the influence of natural ionizing radiation on biological processes during the 30's and 40's, within the framework of aviation medicine studies began to be sucessfully developed on the influence of extreme environmental factors (acceleration, changes in barometric pressure, sharp fluctuations in temperature, etc.) on the organism. The results of these studies were later used in the preparation and conduct of experiments with mammals on ballistic rockets and artificial Earth satellites.

The beginning of the existence of space biology as an independent discipline must apparently be related to the time when the practical need arose to solve the problems associated with manned space flight. The capability of highly organized animals to withstand the effects of ascent, descent and landing of spacecraft had to be tested, the operation of biotelemetric systems and life-support systems had to be checked.

In order to solve these problems, animal rocket flight experiments were conducted in the USSR from the mid-40's through the mid-50's.

Based on recordings of a number of physiological indicators of the animals made during these flights, it was concluded that no significant disorders arose in the organism during brief periods of weightlessness, launch and free-fall with subsequent parachute landing on Earth.

As before, great attention was given during this time to clarification of the biological effectiveness of primary cosmic radiation.

One important stage in the development of space biology was the orbital space flight of Layka, the dog aboard Sputnik-2 in 1957. Analysis of the results obtained during this flight confirmed the assumption of Soviet scientists of the possibility of extended existence of highly organized living organisms under conditions of weightlessness (Gazenko et al. 1962).

The years immediately preceding the first human flight in space, the flight of Yu. A. Gagarin, were a period of intensive development in our country of studies in the area of space biology. /464
This was particularly facilitated by the creation of recoverable satellites (KKC). The experimental objects sent up in recoverable satellites included organisms of widely varied taxonomic levels, from viruses to mammals, allowing us to study the influence of space flight factors, particularly weightlessness, not only on an entire organism, but also at the tissue, cellular and subcellular levels. These experiments turned particular attention to genetic investigations -- the study of the influence of space flight factors on the hereditary structure of somatic and embryonic cells of various organisms.

The importance of studies performed on dogs in flights of returnable satellites was primarily the opportunity they provided to check the medical equipment installed on these spacecraft to moniter the physiological functions of the astronauts, and also to check the human life-support systems.

The analysis of the scientific results obtained by examination of the dogs and other biological objects onboard the returnable satellites made safe space flight possible for man and at the same time revealed certain reversible changes in vital processes (Antipov et al.,1962; Gazenko et al., 1962; Gyurdzhan et al., 1962; Glembotskiy et al, 1962; Dubinin et al., 1962 and others).

These results provided an impetus for further studies in the area of space biology, designed to reveal the essence and mechanism of the changes in vital activity occurring during space flight. These studies were performed in the USSR in orbital flights.

The Academy of Sciences, USSR, as well as other departments of our country, made great contributions to the development of problems of space biology.

## Studies with Mammals and Turtles

Behavior of the animals and the central nervous system. General observations of dogs during experiments aboard rockets and satellites showed no significant changes in their behavior. Disquiet and motor excitation appeared only during the powered flight segments, during periods of maximum acceleration and vibration, and to a lesser extent at the time of motor cutoff, and also ejection. During weightlessness, which lasted 5-10 minutes on the rocket flights and 22 days during satellite experiments, the dogs reacted adequately to the external stimuli. Following the flights, their behavior was also normal (Gazenko et al., 1964; Parin, Pravetskiy, 1968).

Recording of the spontaneous motor activity of rats during the 22-day flight of the Kosmos-605 satellite indicated a gradual reduction in the number of motions during feeding during the course of the flight, which might indicate a reduction in nutritive excitation of the rats under weightless conditions.

No significant disruptions of the coordination of motions of animals in the weightless state on satellite flights or during the post-flight period were observed (Antipov et al., 1962; Kas'yan, 1968). As concerns the clear motor function disorders of the dogs following the 22-day flight of Kosmos-110, it apparently resulted not so much from the influence of extended weightlessness as from the rigid fixation of the animals in the cabin (Parin, Pravetskiy, 1968).

This assumption is supported by the conservation of normal coordination of the motions of rats exposed to weightlessness for the same period of time in a free (unfixed) position. /465

Studies of the condition of the muscular system indicated a reduction in the tonus of the inferior straight muscle of the eyeball of the rabbit following (5 minutes) weightlessness (Yuganov et al., 1968a, b). Following 22 days of exposure of rats to weightlessness, Z. I. Apanasenko detected a suppression of the electrical activity of the posterior group of muscles of the femur. According to V. S. Oganov et al., these same rats showed a reduction in the functional effectiveness of the long digital extensor and the musculus soleus.

Studies of the vestibular tonic reaction of rabbits exposed to brief weightlessness (5 minutes), of guinea pigs following a one-day orbital flight on KKS-4 and of rats following a 22-day flight on the Kosmos-605 biosatellite indicated high sensitivity of the vestibular analyzer to weightlessness.

Analysis of the condition of higher nervous activity showed that following one days's orbital flight, there were no changes in the conditioned reflex activity of rats (Luk'yanova, 1962). Following 22 days exposure to space flight conditions, rats, according to the data of N. N. Livshits et al., manifested changes indicating some depression of the function of the higher segments of the central nervous system.

The cardiovascular system. During studies with dogs performed on rockets and Earth satellites, the condition of the animals was tested using the activity of the cardiovascular system as an indication of general condition. This was a result of the significant role of the circulatory system in the maintenance of normal functioning of the organism, as well as the relative simplicity of the technical system required to measure, record and transmit this information to Earth (Parin, 1967).

It was shown that during the accelerations at launch, the pulse frequency almost tripled. Normalization of the pulse frequency following the transition to weightlessness required almost three times as long as had been required during centrifuge testing on Earth with the same degree of acceleration (Balakhovskiy et al., 1962; Gazenko et al., 1964). This generally occurred during the third or fourth revolution of the flight, after which the pulse frequency stabilized under weightless conditions at a level even lower than the preflight level, indicating the relative predominance of the parasympathetic nervous system tonus. The increase in parasympathetic nervous system tonus under weightless conditions was also indicated by the detection of an increase in the duration of the 0-1 interval, a tendency toward vegotonic reactions during artificial injection of food, and the increase in the difference between the duration of the cardiac cycle between inhalation and exhalation -- "cosmic" arrhythmia -- in the dogs Ugolek and Veterok.

One characteristic peculiarity in the regulation of rhythm of cardiac contractions observed under weightless conditions in all dogs was an increase in the varability of the pulse.

Analysis of the changes in the EKG's of the dogs revealed no pathological changes resulting from weightlessness (Balakhovskiy et al., 1962; Gazenko et al., 1964; Parin, 1966). However, the use

of the polycardiographic method of analysis of cardiac activity indicated some restructuring of the process of heart contraction in the dogs under weightless conditions -- discoordination in the functioning of the right and left sections of the heart (in the dog Pchelka), an increase in the duration of the period of stress and a decrease in the duration of the period of expulsion in the dogs Belka, Pchelka, Ugolek and Veterok (Parin et al., 1967; /466
Kiselev, Nikolayev, 1967).

Measurements of arterial pressure showed that during the takeoff, systolic pressure increased by 20-60 mm Hg, while diastolic pressure increased by 10-20 mm Hg. After 20-60 seconds under weightlessness, a gradual return of arterial pressure to the normal level was observed.

Following 22 days in weightlessness, indications of cardiovascular system detraining were observed in the dogs Veterok and Ugolek (Kiselev et atl., 1967, Kiselev, Nikolayev, 1967; Parin, Pravetskiy, 1968).

Thus, the studies of the cardiovascular system function of dogs showed that weightlessness causes restructuring of the regulation of activity in this system, manifested as an increase in parasympathetic nervous system tonus and a change in the contractive function of the myocardium.

Hematological studies. It was shown that even brief space flight on a rocket caused an increase in the number of leukocytes in the peripheral blood of dogs (Kas'yan et al., 1962). Later, neutrophilic leukocytosis was found in dogs (Zhuravleva, 1967) and rats (L. V. Serova) following 22 days flight in orbit around the Earth.

Normalization of the number of leukocytes in rats occurred after 2-3 days following completion of a flight. In the dogs Ugolek and Veterok (Kosmos-110), full restoration of the initial number of leukocytes still had not occurred 30 days after the end of the flight, which, along with the increased erythrocyte sedimentation rate, indicated some inflamatory process in the organism of these dogs.

Another typical reaction of the peripheral blood to the influence of the complex of space flight factors, apparently, is lymphopenia and erythrocytosis, detected in the blood of dogs and rats immediately after a 22-day flight.

The dyanmics of the change in the remaining indicators of the peripheral blood of dogs and rats exposed to space flight conditions for the same period of time (22 days) were different. For example, the dogs showed an increase in the concentration of hemoglobin, and increase the hematocrit and eosinopenia. The rats, however, showed no changes in the concentration of hemoglobin or in the hematocrit, while a reduction in the number of reticulocytes and an increase in the number of eosinophils were observed.

Following the space flights of KKS-2, 4 and 5, no significant changes were observed in the peripheral blood of the mice carried on these satellites (Arsen'yev et al., 1962).

Very interesting data have been developed on the influence of space flight factors on the function of the hematogenic organs. The most complete information on this problem was produced by examination of the bone marrow and spleen following the flight of mice on KKS-2 and the flight of rats on Kosmos-605. For example, mice sacrificed on the 30th day after the flight showed a definite rejuvenation of the white growth of the bone marrow, manifested as an increase in the number of myeloblasts, promyelocytes and myelocytes. At the same time, a sharp depression in the red growth of the bone marrow and an increase in the numer of chromosome rearrangements were observed. Studies of the spleens of the mice in the early period after the flight (up to the 10th day) indicated a depression of lymphogenesis and myelogenesis, changing to restoration by the 30th day (Arsen'yeva et al., 1962).

Studies of the bone marrow of rats following 20 days space flight, according to the data of L. V. Serova and M. P. Kalandarova, indicated some decrease in the portion of cells of the arythroblastic growth and lymphoid elements, as well as a slight increase in the number of myeloblastic elements and young forms of granulocytes. The total number of bone marrow cells was decreased by 20% in comparison with the control. The bone marrow also showed pathologically changed megakaryocytes, not encountered in the control animals. No clear changes in the mytotic activity of bone marrow cells were observed. /467

A decrease in the number of elements of the erythroid and lymphocytary series was also noted by V. V. Portugalov et al. in their cytological studies of rat spleens.

Twenty-five days after completion of the flight of Kosmos-605, no changes in the blood system of the rats were observed.

Metabolism. During rocket flights, with extreme factors generated by the takeoff, descent and landing acting on the organism during compressed periods of time, changes in metabolism associated with the development of stress reactions occurred. This was indicated by a certain decrease in the blood coagulation time with an increase in the level of prothrombin and the number of thrombocytes, an increase in the content of calcium in the blood, etc. (Gyurdzhian et al., 1961; Kas'yan et al., 1962). These changes normalized again relatively rapidly.

Increasing the time between takeoff and descent to 1.5-3 hours, with the animals exposed to weightless conditions during this time in orbital flight, caused no significant additional changes. As after rocket flights, changes were noted in the metabolism indicating the development of a stress reaction. Unfortunately, these studies were not standardized and therefore cannot be quantitatively compared.

An the time of orbital space flight was increased to a few days, temporary changes were observed in the relationships of protein fractions in the blood serum of dogs and mice, plus a reduction in the content of serotonin in the blood of dogs, temporary protein and fat dystrophy in the myocardium of mice, granular and fat dystrophy in the liver cells of mice (Gyurdzhian et al., 1962; Petrukhin, 1962, Shashkov et al., 1962). These changes disappeared a few days after flights.

Hystochemical studies of the tissues and organs of turtles following space flights of up to 6.5 days showed no clear changes esulting from the influence of weightlessness (Gaydamakin et al., 1969). An increase in the time of weightlessness to 22 days (the dogs Ugolek and Veterok) caused a signficant weight loss of the animals (up to 29% of their launch weight). In this case, in addition to dehydration of the organism, a significant loss of muscle mass was observed (∿15% of body weight). Also observed were hypercalcemia, a decrease in the mineral content of the bone tissue and a negative potassium balance during the first few days after landing. During this same time, the blood serum showed a reduced total quantity of protein, a shart reduction in the relative content of the albumin fraction and a somewhat elevated content of cholesterin in the blood. In spite of the normalization of the overall protein content of the blood by the 9th day after landing, the albumin-globulin coefficient remained significantly reduced.

These changes did not return fully to normal even after a month following the flight, although the weight of the dogs was restored rather quickly. During the post-flight period, the dogs showed moderate hypoglycemia for 3-4 weeks (Parin, Pravetskiy, 1968).

Biochemical studies of the blood of rats following the 22-day flight of Kosmos-605 performed by R. A. Tigranyan et al. showed no significant changes in protein metabolism in the organism. In particular, there were no changes in those blood indicators, except for the proteolysis coefficient, which might indicate proc- /468
esses of tissue catabolism.

The studies of carbohydrate and lipoid metabolism performed by M. S. Gayevskaya et al. on these same rats also showed no significant changes.

Thus, comparative analysis of the results indicates that changes in the metabolism indicators depend not so much on the duration of a space flight as on the conditions of support of the animals on the spacecraft and, possibly, on the species of experimental animals.

Morphological studies. Pathological anatomical examination of a large group of rats following the 22-day flight of Kosmos-605 conducted by V. V. Portugalov et al. indicated no macroscopically visible pathological changes resulting from the influence of space flight factors. All of the internal organs and the endocrine glands were identical in the experimental and control groups, with the exception of the spleen and thymus, which were lighter in the experimental animals, and the adrenals and kidneys, which were heavier in the experimental animals.

No noticeable pathological changes in the valve apparatus of the heart and myocardium of the rats were found. The content of hemosiderophages was the same in the tissues of the lungs of rats in the experimental and control groups.

The first definite selective influence of extended weightlessness on different muscles, observed in the examination of rats following the flight of Kosmos-605, is worthy of attention. It was found that 22 days exposure to weightless conditions caused the development of atrophic and dystrophic processes in the red muscle fibers of the soleus muscle. In a muscle with mixed fiber types -- the long digital extensor -- atrophic processes developed by no dystrophic processes were observed. No morphological changes were observed in any of the other muscles.

The presence of atrophic and dystrophic processes in individual skeletal muscles was observed upon examination of turtles following the flight of Kosmos-605.

As concerns earlier morphological studies on mice after one-day flights on KKS-2 and 6.5-day flights on Zond-5 and 7. due to the brevity of these flights and the limited number of experimental animals, the results produced in these studies must be considered quite approximate (Antipov et al., 1962; Arsen'yeva et al., 1962; Petrukhin, 1962, Gaydamakin et al., 1969).

## Experiments on Insects and Amphibians

Tests with drosophila have been extensively conducted during satellite flights. The frequency of development of recessive lethal mutations in the sex chromosome of males was determined during flights of 12 spacecraft. The experiments were usually performed on two lines of Dr. melanogaster -- high- and low-mutability lines. Wherever possible, i. e. if the duration of the flight was not too great, embryonic cells were analyzed individually for the stages of mature spermia and spermatids. Statistically reliable increases in the frequency of recessive lethals were observed in three experiments. In the other experiments, this effect was not present. No correlation between flight duration and the magnitude or even presence of the genetic effect has been established. Exposure of drosophila in various stages (eggs, larvae, imago) had no influence on the nature of the effect. The use of the radioprotector 5-methoxytryptamine had no influence on the /469 frequency of mutations (Glembotskiy, Parfenov, 1967; Glembotskiy, 1970).

As concerns primary nondivision of sex chromosomes in female drosophila, statistically reliable differences between experimental and control groups occurred in two cases. Near-reliable results were achieved in another experiment. In two more experiments, no differences were noted (Dubinin, 1967). The independence of the effect of flight duration makes it improbable that nondivision of chromosomes is induced by weightlessness. Similar results were produced in two more tests with drosophila -- induced crossing over in males and dominant lethals in females. In a word, the experiments with drosophila showed that weightlessness is not a mutagenic factor for practically all types of mutations.

In the flights of Vostok-3 and Vostok-4, after the satellites were injected into orbit, the cosmonauts crossed virgin female drosophila with males. These experiments showed that copulation, laying of eggs, embryonal and larval development of drosophila occurred normally under weightless conditions. Morphoses were noted, but their nature was nonspecific, and the variation from the normal level was statistically unreliable. Experiments on the development of drosophila in weightlessness were successfully conducted upon Kosmos-605. In these experiments, two normal generations of drosophila were produced in 22 days of weightlessness. The first generation was exposed to weightlessness beginning at an age of 3 days, while the second completed its full cycle of development. The first and second generations could be distinguished by phenotype. The frequency of recessive lethals and nondivision of chromosomes was similar in experimental and control groups.

The dark mealworm beetle carried onboard Kosmos-605 could not complete a full cycle of development, which requires over a month. Therefore, individuals of this species were placed onboard the spacecraft in various stages of development -- from eggs to pupae. Under weightless conditions, the individuals in all stages developed normally and completed the transition to subsequent stages.

These experiments with drosophila and beetles showed that the force of gravity is not required for completely normal of species with centrolecithal egg cells and full type division. We should note here also that no anomalies of embryonal development were noted when the eggs of the parascaris equorum were exposed to weightlessness.

Apparently, the situation is quite different for the eggs of amphibians (frogs). Although the development of the frog egg cells fertilized several hours before the launch occurred practically normally, laboratory experiments on clinostats showed that differentiation into animal and vegetative poles probably requires convection in the fertilized egg cell, which is not present under weightless conditions.

Experiments on Plants

Most studies of the influence of space flight factors on plants have been performed on seeds. Dormant seeds are a convenient object for this purpose. The processes of metabolism are greatly suppressed, and the nucleii in the meristamatic tissue are primarily in one state of development -- the interphase. Damage arising in the chromosomes under the influence of various factors is accumulated and conserved until the moment of germination. During the first mytotic divisions occurring in various objects as a certain sprout length is achieved, nuclear damage can be considered.

By the time the first satellite was launched, it was known from radiation genetics that seeds of various plant groups differ in their sensitivity to the effects of ionizing radiation. Great differences were found not only between families, but also among lower systematic categories such as genus, species and even variety and sort. /470

The data produced in psychological studies of nuclear disruptions in seeds of various species and varieties carried on spacecraft are difficult to systematize. In some objects after flights disruptions are noted in the hereditary structures, while in others they are not noted. The genetic effects recorded in one flight were frequently not repeated in others. It is difficult at present to indicate the reasons for this disagreement of results produced. Some authors believe that the differences can be explained primarily by differences in the initial physiological state of the exposed seeds and, consequently, different reactions to the space flight factors (Antipov et al., 1963). We can assume that comparative analysis would show methodological inaccuracies: for example, the fixed material of the experimental and control groups might not be at identical stages of primary mitoses, resulting in the recording of material which is not identical. We know that after irradiation or exposure to chemical mutagens, the yield of chromosome mutations in the cells of the first mitoses change with growth of the first rootlet. The possibility cannot be excluded that this phenomenon occurs in sprouts growing from seeds subjected to the influence of space flight factors. Therefore, it is important to consider changes in chromosomes in sprouts fixed not at one point in primary mitosis, but throughout the entire cycle at certain time intervals. It is possible that the differences observed in genetic effects of various species of seeds after flight result from oversights during various periods of primary mitosis. It should be noted that the duration of the cellular cycle and of its individual phases was not determined for all species of seeds sent into space, although this is necessary for proper fixation of material in time.

It was noted above that in dry seeds of various plant groups, the cells are primarily in the interphase stage. However, the seeds may be in different phases of this stage, and depending on which phase the seed is in upon exposure to an external effect, rearrangements of various types occur, resulting from the structure of the chromosomes in these phases. Probably for this reason, in some cultures following orbital flights chromatid rearrangements are observed, while in others -- chromosome rearrangements are found. In order to understand the results of experiments and interpret them properly, it is very important to know the occurrence of the natural mutation process in seeds considering the influence of temperature, humidity and age of the seeds. In many species of seeds taken in flights, the natural mutation process was never studied.

When air-dry seeds were exposed onboard satellites, the influence of space flight factors on the processes of growth and

development of plants was determined (Sidorov, Sokolov, 1962; Khvostova et al., 1962; Delone et al., 1967). These observations were made partially as parts of experiments to determine the genetic effects following flights, and in some experiments where the primary task was specially set. Most plants indicated a stimulating effect of space flight factors, manifested in accelerated growth and development processes, as well as increased harvest. Some plants showed only a tendency toward stimulation, and in some cases depression occurred. Researchers believe that it is not presently possible to state just which flight factor causes the stimulation, since the influence of each factor indiviually on the /471
growth processes of plant organisms has not yet been sufficiently studied.

Although it is known that ionizing radiation can rarely cause stimulating effects in plants after irradiation of seeds with doses of radiation which are much lower than lethal doses, the radiostimulating doses for some species fluctuate from a few hundreds to thousands of roentgens. These are not small doses -- on the order of a billion or more rad -- encountered by biological objects during flights on spaceships. It is therefore improbable that the stimulating effect detected in plants grown from seeds carried on spacecraft is related to the effects of cosmic radiation. Also, the stimulation of growth does not correlate to flight duration or the amount of radiation absorbed. Based on the available data on radiostimulation, it also seems to us that even in combination with other flight factors, these doses could hardly cause the stimulation and other changes observed in the growth processes.

Possibly such secondary flight factors as temperature, which changes in certain flight stages, might be one of the agents influencing the growth processes. In particular, it has been experimentally proven that the entire spectrum of changes observed in tradescantia after space flight, including spherical fragments and disruption of mitoses, can be reproduced by moderate temperature influence.

Experiments on Microorganisms and Tissue Cultures

Single-celled organisms are convenient objects for the study of various environmental factors. Therefore, microorganisms were used to blaze the first space trails before the first manned space fight. Later, they were used in independent scientific studies designed to determine the influence of such basic flight factors as weightlessness, ionizing radiation and the combination of these two factors. In spite of the slightly contradictory nature of the data produced, they indicate basically that weightlessness has no direct influence on the growth, development, cell division and mutagenesis of microorganisms, and also does not modify the radiation effect.

The question of the influence of weightlessness on subcellular structures of microorganisms remains open today. For example, according to the data of Zhukov-Verezhnikov et al. (1961), space flight factors resulted in statistically reliable increases in phagoproduction. However, the results of the experiments of R. Mattoni (1968) indicate a depression of Phagoproduction.

The effects observed are explained by the experimenters by the fact that weightlessness influences subcellular processes in bacteria and disrupts the interaction between chromosomes and episomes.

Based on the physical nature of gravitation and considering the generally accepted model of the interaction of chromosomes and episomes in bacteria, it is difficult at present to formulate a scientifically well-founded hypothesis concerning the mechanism of the influence of weightlessness on the genetic structures of the bacterial cell. Furthermore, mathematical calculations performed by E. Pollard show that weightlessness should have no influence on the genetic structure of bacteria. According to the calculations of Pollard, weightlessness might influence cellular metabolism and, consequently, the functioning of subcellular structures, only in cells over 10 μ is diameter. As we know, the diameter of a bacterial cell is significantly less. It varies from 1.5 to 2 μ is diameter, and 2.5 to 6 μ in length. /47?

An experiment with E. coli in the 2-day flight of Soyuz-12 was designed to clarify this question. Microorganisms were carried onboard the spacecraft in a special device to allow the possibility of active multiplication under weightless conditions.

Analysis showed that the number of bacterial cells increased during the time of the experiment by 4-5 orders of magnitude. The increase in the number of cells in a control kept under similar conditions was approximately the same. It was also established that weightlessness had practically no influence on the processes of genetic recombination, reparation and mutagenesis of the bacteria. Investigation of phagoproduction of lysogenic bacteria in this experiment showed that, within the limits of the resolving capacity of the method, phagoproduction on the Earth and under weightless conditions was the same.

The use of tissue cultures to study the influence of space flight factors on the physiology and structural organization of cells in our country was begun in 1960 on the flight of KKS-2 (Zhukov-Verezhnikov et al., 1961). Since this time, practically all experimental satellites, as well as the Vostok and Voskhod spacecraft, have carried experiments with tissue cultures. In spite of the large number of such experiments, performed both in our country and abroad, no clear answer has yet been achieved to the question of the influence of weightlessness on animal cells. The reason for this is apparently the uncontollable and not always identical conditions under which the experiments have been performed. In most cases, cell cultures were carried on the flights under conditions of discomfort and the influence of many factors was studied simultaneously, the effects of which might mask changes resulting from weightlessness. One such factor has been temperature, which has fluctuated in most flights over wide limits, has been far from optimal and was not even recorded. However, as we know, temperature causes cytophysiological and structural changes in cells in tissue cultures and determines the nature of the cellular population restored after cooling or heating.

In general, the results presented indicate that space flight factors do not cause pathological changes in the organism. As concerns the changes which were detected, they do not extend beyond the limits of physiological fluctuations and are not irreversible in nature. Probably the only irreversible phenomenon is possible damage to cerebral nerve cells by high-energy galactic cosmic radiation particles -- protons and heavy ions.

Naturally, weightlessness is of the greatest practical interest of all space flight factors at the present time. Unfortunately, we must report that space biology has as yet succeeded in giving no unambiguous answer concerning the influence of weightlessness on the fundamental vital processes. We can consider it proven only that: 1) weightlessness has its primary influence on those systems of the organism, the functioning of which is related to the force of gravity to some extent under normal conditions (vestibular analyzer, cardiovascular system, musclo-skeletal apparatus, blood system); 2) weightlessness has no mutagenic properties and does not result in the development of mutations in the organisms, at least gene-type mutations; 3) weightlessness is not a development-determining factor for centrolecithal eggs with holoblastic embryogenesis; 4) weightlessness has no influence on the cells and introcellular processes of bacteria, due to the small size of their cells; 5) weightlessness has not influence on cells in which processes of metabolism are either greatly retarded or temporarily stopped; 6) there is no direct dependence between the duration of exposure to weightlessness and the degree of /473 manifestation of various changes detected in the organism.

In connection with the creation of long-lived, large orbital stations, the possibility for the conduct of physiological and biochemical studies with human subjects directly under weightless conditions have significantly expanded. Considering this, it is desirable, in conducting further biological experiments in space, to follow the path not of studying the phenomenology of development of various changes, but rather to concentrate forces on understanding of the intimate mechanisms which serve as the basis of phenomena already established and theoretically presumed. In other words, this means that we can consider justified only studies in space which, for some reason or another, cannot be performed with human subjects.

There, of greatest interest are experimental studies which allow final answers to be given to the questions of the influence of weightlessness on the structural and functional organization of the cell.

Since the biological processes in a cell involve certain intracellular structures, it is important first of all to determine the spatial distribution of these structures and establish whether they sedimentate in the cell under terrestrial gravitational conditions. Mathematical calculations have shown that if the cell cytoplasm is considered a stable medium in which the only factor preventing sedimentation is Brownian motion, in cells of ordinary size at 1 g only cytoplasmatic structures of at least 0.2 $\mu$ in diameter will precipitate. These are the mitochondria, nucleus and plastides in plant cells. Particles of atomic and molecular size apparently are not influenced by terrestiral gravity, since it is significantly weaker than the molecular and electric forces acting in the cell.

It is therefore assumed that the gravitational field of the Earth has no influence on molecular processes, the diffusion of liquids and gases, or chemical reactions catalysed by enzymes. This means that weightlessness should not influence these processes. Actually, the results of properly performed flight experiments on microorganisms and drosophila agree well with these theoretical statements and indicate that intracellular processes are gravity-independent.

Nevertheless, this question still awaits its final answer in future flight experiments. The pressing nature of this type of investigation is indicated by the decrease in the number of erythroid and lymphoid cells in the bone marrow and spleen of experimental rats following 22 days exposure to wieghtlessness, the appearance of pathologically altered megakariocytes in the bone marrow, and also atrophic and dystrophic processes in the cells of certain skeletal muscles.

This trend of investigation is close related to another, no less interesting from the theoretical and practical standpoint, namely the study of processes of growth, development and aging under weightless conditions.

This trend of investigations should be based primarily on the study of the cycle of cell division and the renewability of reproductive tissues of the organism under weightless conditions. Based on theoretical calculations of E. Pollard (1965), we can assume that weightlessness should not be an indifferent factor in relationship to the cycle of cell division, since, as we know, cell division is related to the formation of supermolecular struc- /474
tures, the dimensions of which are greater than a few microns.

In addition to the study of weightlessness as such, biological investigations of the combined influence of weightlessness and other space flight factors, particularly ionizing radiation, are of great interest. It is important to determine the radiosensitivity of organisms in weightlessness, and also to determine the peculiarities of the formation of radiation damage and subsequent restoration of damaged functions in animals and plants under weightless conditions.

The only method of solution of these problems is the irradiation of biological objects in flight by an artificial source of radiation carried onboard a satellite. The results of this type of experiment, in combination with the results of flight radiation physical investigations, will allow the danger of radiation damage for man under conditions of extended weightlessness to be determined, providing a basis for setting of permissible levels of irradiation on long space flights and calculation of the required thickness of radiation shielding around manned spacecraft.

Another important trend of investigations in space is the study of the biological effects of protons and heavy ions from galactic cosmic radiation. These studies can be performed in experiments with seeds, microorganisms, insects and mammals.

Space flight also provides a unique opportunity for the study of processes in the organism which are characterized by daily cyclical changes. It has been established that the complex of geophysical environmental factors influences these processes, including the rotation of the Earth around its axis. In order to understand the true significance of these so-called exogenic factors in the cyclical processes of the organism, biological experiments must be performed during space flights, since only on space flights is partial or complete elimination of the influence of geophysical factors of the Earth possible.

The age of space flight has allowed biologists to study the nature and reaction of living organisms under ecological conditions earlier unavailable for study and has also opened areas of biological investigation in which present theories cannot yield predictions worthy of confidence. Since terrestrial organisms have never encountered environmental conditions such as these characteristic for space flights throughout the entire history of their existence and evolution, space biology has a unique opportunity to study basic questions of biological science, particularly to study the principles of the vital activity of terrestrial organisms.

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